SLOW DELAYED RECTIFIER POTASSIUM CURRENT OF THE ZEBRAFISH (DANIO RERIO) HEART

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Zebrafish is increasingly used as a model for human cardiac electrophysiology, arrhythmias and drug screening. However, K^+ ion channels, which underlie repolarization and determine duration of cardiac action potential (AP) are still incompletely known and characterized. Here we provide the first evidence for the presence of the slow component of the delayed rectifier (Kv7.1) channels in zebrafish heart and investigate the electrophysiological properties of the slow component of the delayed rectifier K^+ current, I_{Ks}.

Atrial and ventricular myocardium show strong transcript expression of the KCNQ1 gene, which encodes the Kv7.1 α-subunit of the slow delayed rectifier K^+ channel. In contrast, the KCNE1 gene, encoding the MinK β-subunit of the delayed rectifier, is expressed 21 and 18 times lower level in ventricle and atrium, respectively, in comparison to KCNQ1. Zebrafish ventricular myocytes regularly demonstrated the rapid component of the delayed rectifier K^+ current, I_{Kr}. Abolition of I_{Kr} with 10 μM E-4031 unmasked I_{Ks} in 62% of ventricular myocytes. The mean density (± SEM) of I_{Ks} was 1.23±0.37 pA/pF at 30 mV, and the time for half-maximal activation of the current at 30 mV was 1248±215 ms. For further characterization of I_{Ks}, KCNQ1 and KCNE1 genes were introduced into Chinese hamster ovary (CHO) cells. CHO cells were transfected with plasmids containing either KCNQ1 or KCNE1 in different proportions (KCNQ1:KCNE1 1:0, 3:1, 1:1, 1:10). CHO cells with 3:1 plasmid ratio generated a current that most closely resembled the native I_{Ks} in kinetic properties. In these cells, the half-activation time was 1725±792 ms at 30 mV. These findings are consistent with the RT-PCR data indicating that KCNQ1 expression strongly prevails over KCNE1 expression, and suggest that not all Kv7.1 α-subunits are associated with MinK β-subunit in zebrafish myocytes. Microelectrode experiments demonstrated the functional relevance of I_{Ks} in zebrafish heart, since 10^{-4}M chromanol 293B produced significant prolongation of AP in zebrafish ventricle.

Thus, AP repolarization in zebrafish ventricle is partly mediated by I_{Ks}, which is mainly generated by Kv7.1 channels not coupled with MinK regulatory subunits. This is a clear difference to the human heart, where MinK is an essential component of the slow delayed rectifier channel.